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Facile catalytic coupling of aryl bromides with terminal alkynes by phospha-palladacycles [1]

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Abstract

An efficient synthesis of tolane derivatives from substituted aryl bromides and phenylacetylene catalyzed by air- and moisture-stable phospha-palladacycles is described. This procedure works without addition of cupric salts. Reaction rates and yields are sensitive to the nature of solvent and base. Mechanistic features are discussed for a catalytic cycle with Pd(II) and Pd(IV) intermediates. Constitutional stability of the palladacyclic catalyst under reaction conditions is likely; precipitation of palladium black is not observed.

Keywords: Palladium; Palladacycles; Acetylenes; Aryl halides; *CC*-coupling

1. Introduction

The palladium-catalyzed coupling of aryl iodides and bromides with terminal acetylenes is a well-established synthetic method for internal alkynes in organic synthesis as reported independently by L. Cassar [1] and R.F. Heck [2]. Internal acetylenes are used as typical structure units in liquid crystals [3] and as common organic building blocks [4]. Furthermore, subsequent hydrogenation with palladium on charcoal results in cis-olefins, which are difficult to synthesize selectively. In industrial applications, however, the relatively high amount of catalyst (1–5 mol% Pd) and the addition of copper(I) iodide (1–5 mol% Cu) as co-catalyst [5] (few exceptions are reported [2,6], [5]b) warrant a complicated catalyst recycling which, for practical considerations, is much too expensive.

In general, palladium-catalyzed reactions [7] employ only a small variety of complexes as catalyst precursors; they are preferentially stabilized by phosphines and lack carbon–metal bonds. Therefore, our objective was to establish the palladacycles 1 as a new structure principle

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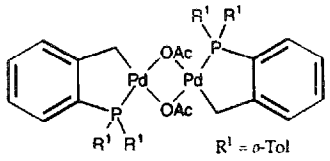
in catalysis [8]. The main advantage of these moisture- and air-stable complexes is the long lifetime, even under severe reaction conditions, without palladium black being formed.



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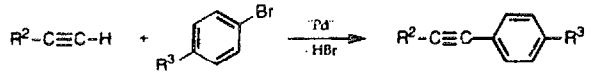
2. Results

We chose the standard system 4-bromoacetophenone/phenylacetylene as to investigate the solvent and base dependence of the coupling reaction when only 0.1–0.5 mol% of the phospha-palladacyle is used. The coupling reactions follow Eq. 1. Surprisingly, only triethylamine as solvent and base gave good yields and the addition of different co-solvents slows down the reaction drastically or inhibits it completely. Table 1 outlines this strong solvent effect, showing that other bases than triethylamine give only poor results.



(1)

This unique effect of triethylamine may be explained by a sensitive association–dissociation equilibrium at the active organopalladium species and the near quantitative precipitation of triethylammonium bromide formed during the reaction.

The higher rates and yields for acceptor-substituted aryl bromides (Tables 1 and 2) are consistent with the oxidative addition step in the beginning of the catalytic cycle. Different substrates show good results for any aryl bromide with phenylacetylene but poor yields with alkyl acetylenes. However, neither the lower reaction temperature for the different alkyl acetylenes (lower boiling points) nor the different acidity of the terminal acetylenes explain their low reactivity in this procedure.

Table 1
Catalytic coupling of phenylacetylene with 4-bromoacetophenone according to Eq. 1

Catalyst 1 [mol%]	Solvent	Base	Temp. [°C]	Time [h]	Yield [a] [%]
0.1	triethylamine [b]	same	90	5	99
0.1	tributylamine	same	90/130	8	12/40
0.1	diethylamine	same	60	7	0
0.1	DMI [c]	same	90	7	0
0.1	pyridine	same	80	9	0
0.1	piperidine	same	90	7	0
0.1	DMAc	NaOAc	80	2	0
0.5	DMAc	tributylamine	130	7	13
0.5	triethylamine	MTBD	80	7	8
0.5	triethylamine	DBU	80	4	7
0.1	triethylamine	NaOMe	78	7	0
0.5	NMP	triethylamine	90	7	10
0.1	acetonitrile	triethylamine	90	9	25
0.5	xylene	triethylamine	90	7	8

[a] GC yield of corresponding coupling product based on aryl bromide.
[b] *Reaction conditions*: 10 mmol aryl bromide, 12 mmol acetylene, 30 ml solvent and 12 mmol base.
[c] *Abbreviations*: DMAc = dimethylacetamide, DMI = 1,3-dimethyl-2-imidazolidinone, NaOAc = sodium acetate, MTBD = 1,3,4,6,7,8-hexahydro-1-methyl-2*H*-pyrimido[1,2-a]pyrimidine, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, NMP = *N*-methylpyrrolidone, NaOMe = sodium methanolate.

Table 2
Catalytic *CC*-coupling of aryl bromides with alkynes according to Eq. 1

Catalyst 1 [mol%]	Aryl bromide	Acetylene	Temp. [°C]	Time [h]	Yield [a] [%]
0.1	4-bromoacetophenone	phenylacetylene	90	5	99
0.01	4-bromoacetophenone	phenylacetylene	90	24	80
0.1	4-bromoacetophenone	propargyl-thp-ether [b]	90	8/24	20/30
0.1	4-bromoacetophenone	trimethylsilylacetylene	90	7	0
0.1	4-bromoacetophenone	propargylic alcohol	70	7	0
0.1	4-bromoacetophenone	propargyl-tms-ether [b]	90	24	20
0.1	4-bromoacetophenone	hex-1-yne	80	9/24	0
0.1	4-chlorobromobenzene	phenylacetylene	90	8/16	80/90
0.1	4-chlorobromobenzene	propargyl-thp-ether	90	36	40
0.1	4-chlorobromobenzene	propargyl-tms-ether	90	38	10
0.1	4-chlorobromobenzene	hex-1-yne	80	9/24	0
0.1	4-*n*-butylbromobenzene	phenylacetylene	90	9/24	60/80
0.1	4-*n*-butylbromobenzene	propargyl-thp-ether	90	24	0
0.1	4-*n*-butylbromobenzene	trimethylsilylacetylene	90	29	0
0.1	4-bromoanisole	phenylacetylene	90	7/24	40/80
0.1	4-bromoanisole	propargyl-thp-ether	90	24	0
0.1	2-bromopyridine	phenylacetylene	90	8/24	20/30
0.1	2-bromopyridine	propargyl-thp-ether	90	24	0

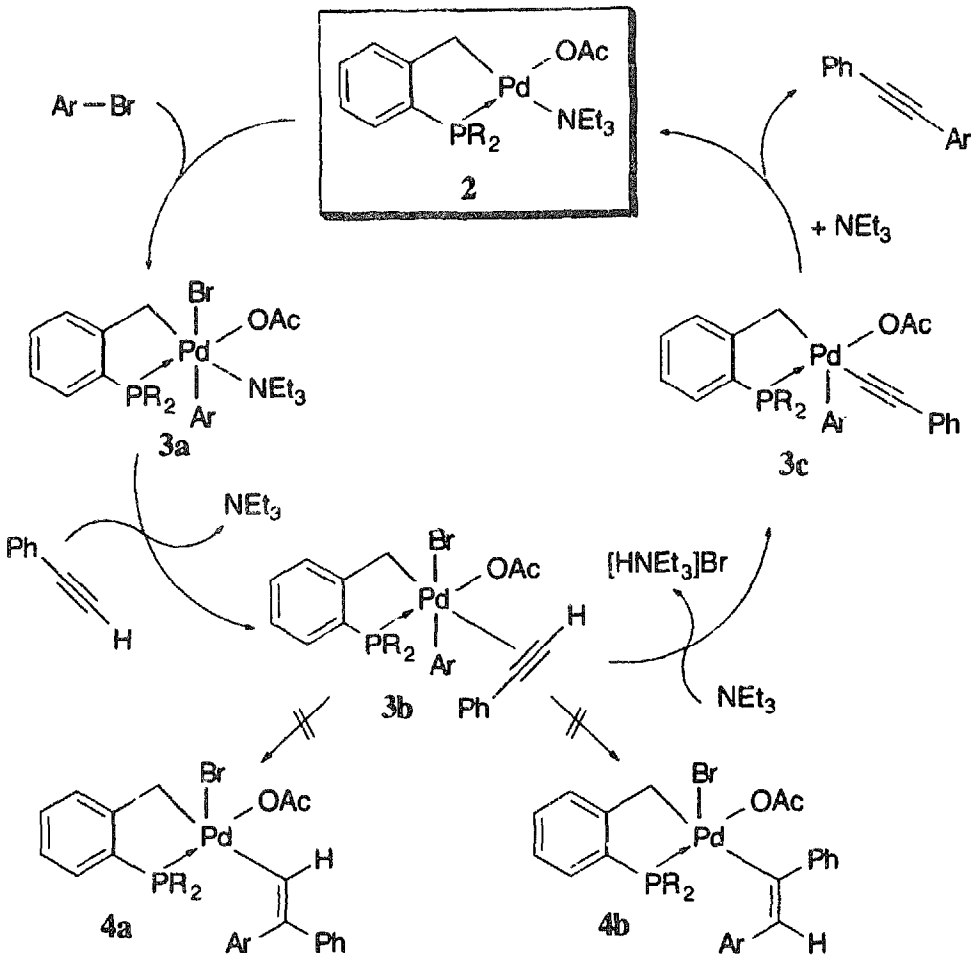
[a] GC yield of corresponding coupling product based on aryl bromide.
[b] *Abbreviations*: thp = tetrahydropyran, tms = trimethylsilyl.

When the amount of palladium in the standard system is further reduced to only 0.01 mol% of catalyst, the turnover number (TON) can be increased to almost 8000 [mol product/mol catalyst] with 80% yield. This enormous activity of the standard system is, to our knowledge, the highest activity reported in the literature for this type of reaction.

3. Discussion

We introduced palladacycles as easy-to-use catalysts for carbon–carbon bond forming reactions such as the Heck and Suzuki reaction [8,9] and have now demonstrated their application in the coupling of aryl bromides with aryl acetylenes. The mechanistic features are not obvious with respect to the oxidation state and structural details of the active species. Both the high stability of the palladacycles and the negligible precipitation of palladium black during catalysis indicate that the structurally intact palladacycles could be the active species [10]. Based on that assumption, a catalytic cycle would involve an oxidative addition step from Pd(II) to Pd(IV), which is not generally accepted although several examples of Pd(IV) complexes are known indeed [11].

One possible catalytic cycle is shown in Scheme 1. Starting from the postulated amine adduct **2**, the acetylide **3c** is a reasonable final intermediate because both vinylic intermediates, such as **4a** and **4b**, have no possibility for common hydrogen elimination steps; we therefore exclude their formation. The obvious driving force is the fast and nearly quantitative replacement of HBr as triethylammonium bromide (step **3b** to **3c**). Additionally, the association–dissociation equilibrium is shown in several steps, where triethylamine plays an important role to regenerate the active species. Furthermore, the acetate ion will not be replaced by bromide at the active site, because triethylammonium acetate is soluble in triethylamine and anionic complexes will not be formed during



Scheme 1. Proposed mechanism of the catalytic coupling reaction.

the reaction. In spite of representing a plausible mechanism, Scheme 1 warrants further verification.

Further studies are aimed at tandem reactions where more than one carbon–carbon bond is formed during one catalytic cycle, thus yielding more complex products.

4. Experimental

Palladium(II) acetate was purchased from DEGUSSA AG. Phosphines and other chemicals were obtained from Aldrich and Fluka. All products were characterized by GC–MS, yields were determined by gas chromatography. Quantitative GC analyses were performed with a Hewlett Packard 5980 A instrument using a 12.5 m HP-1 capillary column in conjunction with a flame ionization detector (GC/FID).

4.1. Catalyst preparation

Palladium acetate (4.5 g, 20.0 mmol) is dissolved in 500 ml of toluene. To the reddish brown solution is added tri(*o*-tolyl)phosphine (8.0 g, 26.3 mmol). The mixture that changes its colour to bright orange is heated at 50°C for 3 min and then rapidly cooled to room temperature. About 375 ml of the solvent are removed in vacuo. To this residue is added 500 ml of hexane which causes the precipitation of the complex. After filtration and drying in vacuo 8.8 g of *trans*-di(μ-acetato)-bis[-*o*-(di-*o*-tolylphosphino)benzyl]dipalladium(II) are obtained as a yellow solid (93% yield referred to

$Pd(OAc)_2$). A solution of the complex in toluene or dichloromethane can be further purified by filtration through a bed of Celite®. Recrystallization from toluene/hexane or dichloromethane/hexane yields the product in a microcrystalline and analytically pure form (yellow crystals).

Elemental analysis: Found.: C, 58.89; H, 5.06; P, 6.92; O, 6.47; Pd, 21.84%. $C_{46}H_{46}P_2O_4Pd_2$ (937.62) calc.: C, 58.93; H, 4.94; P, 6.61; O, 6.83; Pd, 22.70%; ^{1}H NMR (400 MHz, −70°C, CD_2Cl_2): δ = 7.31 (4H, m, H_{tolyl}); 7.21 (2H, m, H_{tolyl}); 7.12 (6H, m, H_{tolyl}); 7.06 (2H, t, H_{benzyl}, ^3J(HH) = 7.3 Hz); 6.92 (4H, m, H_{tolyl}); 6.70 (2H, t, H_{benzyl}, ^3J(HH) = 7.3 Hz); 6.56 (2H, t, H_{benzyl}, ^3J(HH) = 9 Hz); 6.35 (2H, dd, H_{benzyl}, ^3J(HH) = 7.9 Hz, ^4J(PH) = 12.2 Hz); 3.00 (6H, s, CH_3), 2.81 (2H, dd, CH_aH_b. $^2J(H_aH_b)$ = 14.0 Hz, ^3J(PH) = 4.5 Hz); 2.40 (2H, dd, CH_aH_b, $^2J(H_aH_b)$ = 14.0 Hz, ^3J(PH) = 1.8 Hz); 2.10 (6H, s, CH_3); 1.91 (s, 6H, CH_3); ^{13}C{^{1}H} NMR (100.5 MHz, −70°C, CD_2Cl_2): δ = 178.5 (s, CH_3CO_2); 157.1 (d, C_{aryl}, J(PC)0 = 31.3 Hz); 141.1 (d, C_{aryl}, J(PC) = 16.0 Hz); 141,0 (d, C_{aryl}, J(PC) = 21.0 Hz); 133.0 (s, C_{aryl}); 132.5 (d, C_{aryl}, J(PC) = 4.6 Hz); 132.4 (d, C_{Ar}, J(PC) = 6.1 Hz); 131.7 (d, C_{Ar}, J(PC) = 8.8 Hz); 131.4 (d, C_{Ar}; J(PC) = 13.7); 131.3 (d, C_{aryl}, J(PC) = 9.9 Hz); 130.4 (d, C_{aryl}, J(PC) = 16.0 Hz); 129.9 (s, C_{aryl}); 129.1 (d, C_{aryl}, J(PC) = 46.2 Hz); 128.7 (s, C_{aryl}); 128.1 (d, C_{aryl}, J(PC) = 33.2 Hz); 127.6 (d, C_{aryl}, J(PC) = 23.7 Hz); 125.6 (d, C_{aryl}, J(PC) = 7.3 Hz); 125.2 (d, C_{aryl}, J(PC) = 7.3 Hz); 124.9 (d, C_{aryl}, J(PC) = 11.4 Hz); 30.8 (s, CH_2); 24.7 (d, CH_3CO_2, ^4J(PC) = 3,1 Hz); 23.0 (d, CH_3, ^3J(PC) = 13.7 Hz); 22.2 (d, CH_3, ^3J(PC) = 6.9 Hz); ^{31}P{^{1}H} NMR (161.9 MHz, −70°C, CD_2Cl_2): δ = 34.2 (s);

4.2. General procedure

In a 100 ml three-necked flask equipped with a septum inlet, a thermometer and a reflux condenser were placed aryl bromide (10 mmol), terminal acetylene (12 mmol), amount of catalyst (R^1 = *o*-Tol), diethyleneglycol-di-*n*-butyl ether (0.2 g, GC standard), and triethylamine (30 ml). The reaction mixture was stirred vigorously and heated to the appropriate reaction temperature. 0.5 ml samples were removed after every hour and sealed in GC vials for the gas chromatographic determination of the yield. The work-up was achieved by filtering of the hot reaction mixture and subsequent cooling of the organic phase. The product was obtained by either crystallization (after several hours at room temperature) or by evaporation of the triethylamine.

4.3. Example

In a 100 ml three-necked flask were placed 2.02 g 4-bromonitrobenzene (10 mmol), 1.2 g phenylacetylene (12 mmol), 10 mg catalyst (R^1 = *o*-Tol), 0.2 g diethyleneglycol-di-*n*-butyl ether (GC standard), and triethylamine (30 ml). The reaction mixture was stirred vigorously and heated to 90°C. After 4 h, the hot reaction mixture was filtered and cooled to room temperature. After 2 h, 1.73 g 1-(4-nitrophenyl)-2-phenylethyne are obtained as a crystalline product (80% yield).

^{1}H NMR (300 MHz, 20°C, $CDCl_3$): δ = 8.2 (2H, m, $H_{ar,nitro}$), 7.66 (2H, m, $H_{ar,nitro}$), 7.56 (2H, m, H_{ar}), 7.39 (2H, m, H_{ar}); ^{13}C{^{1}H} NMR (75.4 MHz, 20°C, $CDCl_3$): δ = 147.0 (s, C–NO_2), 132.6 (s, C_{ar}), 132.3 (s, C_{ar}), 131.9 (s, C_{ar}), 130.3 (s, C_{ar}), 129.3 (s, C_{ar}), 128.6 (s, C_{ar}), 125.0 (s, C_{ar}), 123.7 (s, C_{ar}), 94.8 (s, $C_{acetylene}$), 87.6 (s, $C_{acetylene}$).

References

[1] L. Cassar, J. Organomet. Chem., 93 (1975) 253.

[2] H.A. Dieck and R.F. Heck, J. Organomet. Chem., 93 (1975) 259.

[3] M. Hird, K.J. Toyne and G.W. Gray, Liq. Cryst. 14 (1993) 741.

[4] (a) T. Sakamoto, H. Nagata, Y. Kondo, M. Shiraiwa and H. Yamanaka, Chem. Pharm. Bull. 35 (1987) 823. (b) A.P. Melissaris and M.H. Litt, J. Org. Chem. 59 (1994) 5818. (c) T. Okita and M. Isobe, Synlett, (1994) 589. (d) T. Okita and M. Isobe, Tetrahedron, 51 (1995) 589.

[5] (a) A.P. Melissaris and M.H. Litt, J. Org. Chem. 57 (1992) 6998. (b) M. Alami, F. Ferri and G. Linstrumelle, Tetrahedron Lett., 34 (1993) 6103. (c) T. Sakamoto, F. Shiga, A. Yasahara, D. Uchiyama Y. Kondo and H. Yamanaka, Synthesis, (1992) 746.

[6] M. Pinault, Y. Frangin, J P. Genêt and H. Zamarlik, Synthesis, (1990) 975.

[7] (a) J. Tsuji, Organic Synthesis with Palladium Compounds, Springer, Berlin, 1980. (b) R.F. Heck, Palladium Reagents in Organic Synthesis, Academic Press, New York, 1985.

[8] (a) W.A. Herrmann, C. Brossmer, K. Öfele, C.-P. Reisinger, T. Priermeier, M. Beller and H. Fischer, Angew. Chem. 107 (1995) 1989; Angew. Chem., Int. Ed. Engl. 34 (1995) 1844. (b) W.A. Herrmann, C. Brossmer, K. Öfele, M. Beller and H. Fischer, J. Mol. Catal., 103 (1995) 133.

[9] M. Beller, H. Fischer, W.A. Herrmann, C. Brossmer and K. Öfele, Angew. Chem. 107 (1995) 1995; Angew. Chem., Int. Ed. Engl. 34 (1995) 1848.

[10] The recovery of the catalyst is restricted by product separation and could not be achieved.

[11] (a) A.J. Canty, Plat. Met. Rev. 37 (1993) 2. (b) B.M. Trost, J. Am. Chem. Soc., 113 (1991) 1850.